Oligonucleotides were tested in EL-4 T cells (ATCC TIB-39, American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110) by Northern blot analysis as described in previous examples using a commercially available murine IL-5 probe. These cells are PHA responsive and PMA plus cAMP elevating agents induce a several hundredfold increase in IL-5 synthesis by these cells. Cells were maintained and stimulated to express IL-5 according to published methods and transfected with oligonucleotide via electroporation.

A1

At page 66, starting at line 22, please replace the paragraph with the following paragraph:

These oligonucleotides were electroporated into human HSB-2 cells and tested for effect on IL-5 mRNA by Northern blot analysis as described in previous examples. The HSB-2 T-cell line was obtained from the American Type Culture Collection (10801 University Boulevard, Manassas, VA 20110) and cells are cultured according to ATCC recommendations. They produce IL-5 upon induction with PMA + ionomycin. Oligonucleotides were tested by Northern blot analysis at a concentration of 10 μM for their ability to block IL-5 mRNA expression. The results are shown in Table 5.

A2

At page 69, starting at line 19, please replace the paragraph with the following paragraph:

--Using an RNAse protection assay (RiboquantJ hCK4, Pharmingen, La Jolla, CA), it was determined that ISIS 16085 inhibited IL-5 expression in a second T cell line, CEM (obtained from American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110) with an IC50 estimated at approximately 25 μM. IL-5 expression is induced in these cells by treatment with PMA plus ionomycin in the presence of IL-2, anti-CD28 cross-linking antibody, and dibutyryl cAMP. Dose response analysis of ISIS 16085 vs. Its 5-mismatch control in stimulated CEM cells showed a dose-dependent decrease in IL-5 mRNA of about 50% at 25 μM oligonucleotide, compared with about 22% reduction with the mismatch control. No decreases were seen in other cytokine gene products measured in this assay.--

A3

At page 73, starting at line 3, replace the paragraph with the following paragraph:

--Murine BCL cells were chosen for screening antisense oligonucleotides targeted to murine IL-5 receptor-a. These are B-cell leukemia cells derived from a spontaneously arising tumor of BALB/c origin, and proliferate in response to murine or human IL-5. This is a CD5+ line which resembles a subset of human chronic lymphocytic leukemia tumors and secretes IgM upon lipopolysaccharide stimulation. Cells were obtained from the

A4